

the group receiving it only orally within the first 24 hours (gr.B, n = 6732). GUSTO tested four regimens of thrombolysis: accelerated t-PA with IV heparin, streptokinase (SK) with IV/subcutaneous heparin and combination of t-PA and SK with IV heparin, in 41,021 patients. Atenolol was administered, if not contraindicated, as two doses of 5 mg. IV, every 15 minutes followed by 50–100 mg. orally every day. In 9987 patients, there were contraindications to its use, as perceived by the enrolling physician. The baseline characteristics of the patients receiving IV atenolol were not unfavorable in terms of previous infarction, Killip class, assignment to t-PA, age, systolic pressure, heart rate or time to treatment, when compared with the whole cohort receiving atenolol within the first 24 hours. The main events are listed below: (CHF — congestive heart failure, v.fib — ventricular fibrillation):

	death-n (%)	CHF (%)	ischemia (%)	v. fib (%)	pacing (%)	shock (%)
gr. A	504 (3.1)	14.3	22.1	5.4	6.0	3.3
gr. B	214 (3.0)	10.7	18.9	4.7	4.0	2.2
p	NS	p < 0.01	p < 0.01	NS	p < 0.01	p < 0.01

There was a similar incidence of reinfarction and angiographic reocclusion in the 2 groups. Although not a randomized comparison, the utilization of IV atenolol in the first 24 hours after myocardial infarction, was paradoxically associated with increased morbidity, when compared to the more gradual oral β blockade.

ACUTE MYOCARDIAL INFARCTION/UNSTABLE ANGINA

901-4 Genetic Predisposition to Neurohumoral Activation Following Myocardial Infarction: Effects of the Angiotensin Converting Enzyme I/D Polymorphism

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Recent studies suggest that a deletion polymorphism of the angiotensin converting enzyme (ACE) gene is associated with increased plasma ACE activity and an increased risk for both, myocardial infarction (MI) and left ventricular hypertrophy (LVH). To test the hypothesis whether the deletion ACE genotype also affects neurohumoral activation following MI, we studied 96 patients, 59 \pm 9 years of age, with acute anterior MI, no overt heart failure, or need for ACE-inhibition. Subjects were randomized to treatment with either captopril or placebo following thrombolytic therapy. Bloodsamples for plasma norepinephrine and ACE activity were taken at baseline (before thrombolysis) and 1, 12 and 24 hours after thrombolysis. ACE genotyping (polymerase chain reaction; specific primers amplifying 190 bp and 490 bp fragments of deletion [D] and insertion [I] alleles, respectively) was carried out at the end of follow-up, without knowledge of clinical parameters. At baseline, norepinephrine levels were equal in DD, I/D and II groups. In contrast, the increase of norepinephrine levels was more pronounced in MI patients with DD (n = 34; 556 \pm 189 pg/ml) as compared to ID and II genotype (n = 62; 96 \pm 98 pg/ml; p < 0.01). Furthermore, baseline ACE activity was higher in the DD genotype group (29 \pm 3 vs 23 \pm 2 U/l; p = 0.01). This increased response in DD genotype patients was blunted by captopril. Association of the DD genotype and adverse neurohumoral activation was still evident after correction for infarct size and captopril treatment (p < 0.01). Thus, the ACE/DD genotype appears to increase the risk for neurohumoral activation after anterior MI and DD genotype patients benefit most from early ACE inhibition.

901-5 Intravenous Amiodarone Restores Sinus Rhythm in Acute Myocardial Infarction Complicated with Atrial Fibrillation

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The effectiveness and tolerance of intravenous (IV) amiodarone (Am) in atrial fibrillation (AF) complicated acute myocardial infarction (AMI) is not well studied. Thus, twenty patients (Pts) with AMI complicated with AF occurring within 30 h (11.9 \pm 10) of the onset of AMI symptoms were treated with IV administration of digitalis (d, 0.5 mg and an additional 0.25 mg later) followed by IV Am 300 mg over 2 h (starting 2 h after the initial dose of d) and followed by 44 mg/h for up to 3 days, if sinus rhythm (SR) was not restored. Intravenous d restored SR within 2 h in 5/20 pts. AF relapsed in 2 of them. Subsequent administration of Am for 2 h restored SR in the remaining 15/20 pts and in the 2 pts in whom AF had relapsed after the initial restoration of SR by d. Am restored SR within an average of 12.8 (range 0.5–56) h of infusion. Total dose of Am was 1922 \pm 720 mg in 4 pts and 425 \pm 241 mg in the remaining 13. Am was well tolerated by all pts including 1 with cardiogenic

shock assisted with the intraaortic balloon pump.

In conclusion, IV Am administration is highly effective in restoring sinus rhythm in AF complicating AMI and is well tolerated.

901-6 Psychophysiological Investigations of Myocardial Ischemia (PIMI): Initial Results on Mechanisms of Cardiac Ischemia

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Psychological factors are linked to outcomes in coronary artery disease (CAD) pts but the mechanisms are obscure. The PIMI is a NIH multicenter study designed to test the overall hypothesis that manifestations and expressions of ischemia are influenced by specific psycho-physiologic mechanisms. Accordingly, 200 pts, mean age 62, with CAD and ischemia responses on treadmill were studied. Ambulatory ECG (AECG) monitoring, psychological instrument batteries and plasma biochemical tests were applied to identify mechanisms associated with ischemia during daily life, exercise and mental stress without influence of cardiac medications. Daily life ischemia (AECG) occurred in 41% of pts (95% with ischemia were asymptomatic) and was associated with lower hostility (p < 0.01) and anger expression (p < 0.03) scores compared with those without daily life ischemia. An inverse association between magnitude of daily life ischemia and these scores was observed. No differences were found for depression (Beck) or anxiety scores. On treadmill all pts had ischemia (ST segment depression) but 44% had angina. Angina expression was associated with higher depression (p = 0.002), anxiety (State, p = 0.002 and Trait, p = 0.01) and autonomic perception (p = 0.05) scores than no angina. Depression best predicted time to angina (Cox model, p = 0.007).

During mental stress (Stroop and speech tasks) ischemia (radionuclide ventriculogram (RVG) or ST segment abnormalities) occurred in 79% of pts (95% with ischemia were asymptomatic) and associated with higher Reward, Dependence, (Temperament and Character Inventory, p < 0.02) and level of irritation during Stroop task (p < 0.01). Plasma norepinephrine remained low, but epinephrine doubled and systolic pressure increased. No associations were found for medical or demographic factors examined. During bicycle exercise ischemia (RVG abnormality) occurred in 94% of pts (64% with ischemia were asymptomatic) yet norepinephrine increased three-fold.

In summary, daily life ischemia (usually asymptomatic) is associated with suppressed hostility, anger and emotion but not depression or anxiety. Mental stress ischemia (mostly asymptomatic and with epinephrine release) is related to temperament characteristics. Exercise stress ischemia, on the other hand, more often evokes symptoms and marked norepinephrine release but symptom expression seems dependent upon depression, anxiety and autonomic perception. Mechanisms responsible for ischemia evoked in different settings and its symptomatic expression involve complex interactions of behavioral, physiological and psychophysiological factors.

ACUTE MYOCARDIAL INFARCTION/UNSTABLE ANGINA — LONG-TERM OUTCOME

901-7 The Survival Advantage of Early Grade 3 Patency After Thrombolysis for Infarction Increases Over Time

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The survival advantage for thrombolytic treated infarct patients who exhibit prompt (90') full coronary patency, grade 3, (versus incomplete, 2, or absent flow, 0,1) is well established at time points of one week or one month. The GUSTO angiographic study now allows inspection of subsequent changes, if any, in the flow grade specific patency-mortality relationships to one full year's follow up. Of 1173 patients in whom infarct artery (IRA) patency grade was established angiographically 90' after treatment was begun, 12 month follow up is available in 99.9% (1172). Patency-1 year mortality relationships were:

